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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SOROUSH, LAYLA	
ART UNIT	PAPER NUMBER
1627	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	09/153,133	LEE ET AL.	
	Examiner	Art Unit	
	LAYLA SOROUSH	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 June 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *45-46, 58--59, 73, 75-77* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *45-46, 58--59, 73, 75-77* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/17/11*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 17, 2011 has been entered. Claims 45-46, 58--59, 73, 75-77 are pending.

See rejections below:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 45-46, 58-59, 73 and 75-77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reyveld (US Patent 4,016,252), in view of Antonucci et al. (5508342) and Gerhard et al. (US Patent 5,085,861).

Relyveld teaches the state of art for using calcium phosphate to improve the efficacy of vaccine formulations. Reyvald teaches injectable gel calcium phosphate vaccine formulations comprising an immunogens from various bacteria (comprise nucleic acid molecules) and viruses (see abstract, col 2, lines 1-5, col 3-4). The calcium to phosphate ratio in gel formulation of Relyveld is from 1.62 to 1.85 (abstract, col 2

lines 1-15, col 3-4). The phosphate of the gel are between those of dicalcium and tricalcium phosphates. Reyveld also teaches mixed vaccines by the addition of a calcium phosphate gel which has adsorbed a specific antigen, to a solution containing one or several other antigens. Therefore, Reyveld teaches the appropriate range of calcium and phosphate concentrations in the final formulation. The vaccines are made to treat patients which encompass humans.

The reference is silent to the amorphous form of the calcium phosphate.

However, Antonucci et al. teaches amorphous calcium phosphate is preferred as the mineralizing agent for the formation of HAP (hydroxyapatite). Because of both thermodynamic and kinetic effects, ACP readily dissolves in aqueous systems to form stable, crystalline structures of HAP, one of the major components of bones and teeth.

Gerhard disclose calcium phosphate containing compositions comprising biocompatible calcium phosphate ceramics that can be in the form of an injectable or moldable paste and will solidify within 10 minutes after administration (see abstract; Col 7, lines 30-46, 60-67; Col 8, lines 1-20; examples 2-3). Gerhard's compositions contain active agents that are readily used in treatment of cancers such as bone tumor (Col 13, lines 45-67).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to modify physical characteristics of Reyveld's composition into an injectable paste, as suggested by Gerhard and Antonucci et al., and formulate a hardenable calcium phosphate formulation that is easily administered to a site of interest and readily dissolves in aqueous systems to form stable crystalline structures of

HAP. One would be motivated to use an amorphous calcium phosphate in an injectable paste because the ordinary artisan would have had a reasonable expectation of success in achieving the same results of ease of administration to a site and readily dissolves in aqueous systems to form stable crystalline structures of HAP.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 45, 46, 58-59, 73 and 75-77 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 56 and 57 of U.S. Patent No. US 6541037 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the invention of the prior art is a vehicle for delivering a biologically active agent comprising: a calcium phosphate source consisting essentially of an amorphous calcium phosphate (ACP) and an acidic calcium phosphate; an aqueous solution in an amount to provide a paste of formable or

injectable consistency with the calcium phosphate source, the paste being capable of hardening in association with an endothermic reaction; and a biologically active agent contained in or on the paste whereas the claims herein are a delivery composition comprising: a) calcium phosphate comprising an amorphous calcium phosphate (ACP) or a poorly crystalline apatitic (PCA) calcium phosphate; and b) an antigen or vaccine wherein said calcium phosphate comprises greater than or equal to 40 wt% of said composition, and wherein said composition is formulated as an injectable paste that hardens in an endothermic reaction.

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate a vaccine or antigen into the composition. The motivation comes from the teaching that a biologically active agent is delivered using the ACP vehicle. Hence a skilled artisan would have reasonable expectation of success to incorporate the biologically active agents, vaccine or antigens.

Claims 45, 46, 58-59, 73 and 75-77 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-21 of U.S. Patent No. US 6214368. Although the conflicting claims are not identical, they are not patentably distinct from each other because the invention of the prior art is a formable paste, suitable for use as a bone substitution material, comprising: a powder comprising a first calcium phosphate material having at least 90% amorphous character and an acidic second calcium phosphate material, the powder having a calcium to phosphorous molar ratio in the range of about 1.2 to 1.68; and a fluid in an amount to provide a formable or injectable consistency, said paste remaining injectable or formable for a

time greater than about 60 minutes at about 22.degree. C. and hardenable within about 30 minutes at about 37.degree. C., said paste suitable for use as a bone substitute material whereas the claims herein are a delivery composition comprising: a) calcium phosphate comprising an amorphous calcium phosphate (ACP) or a poorly crystalline apatitic (PCA) calcium phosphate; and b) an antigen or vaccine wherein said calcium phosphate comprises greater than or equal to 40 wt% of said composition, and wherein said composition is formulated as an injectable paste that hardens in an endothermic reaction.

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate a vaccine or antigen into the composition. The motivation comes from the teaching that a biologically active agent is delivered using the ACP vehicle. Hence a skilled artisan would have reasonable expectation of success to incorporate the biologically active agents, vaccine or antigens.

Claims 45, 46, 58-59, 73 and 75-77 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. US 5676976. Although the conflicting claims are not identical, they are not patentably distinct from each other because the invention of the prior art is a method of preparing a reactive amorphous calcium phosphate, comprising: precipitating a carbonated amorphous calcium phosphate from an aqueous solution comprising calcium ions, phosphate ions and carbonate ions; and heating the carbonated amorphous calcium phosphate under conditions selected to remove at least a portion of residual water and at least a portion of the carbonate ion while retaining the amorphous

character of the calcium phosphate, whereby a reactive amorphous calcium phosphate is obtained whereas the claims herein are a delivery composition comprising: a) calcium phosphate comprising an amorphous calcium phosphate (ACP) or a poorly crystalline apatitic (PCA) calcium phosphate; and b) an antigen or vaccine wherein said calcium phosphate comprises greater than or equal to 40 wt% of said composition, and wherein said composition is formulated as an injectable paste that hardens in an endothermic reaction.

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate a vaccine or antigen into the composition. The motivation comes from the teaching that a biologically active agent (is useful -- see specification) is delivered with the ACP. Hence a skilled artisan would have reasonable expectation of success to incorporate the biologically active agents, vaccine or antigens.

Claims 45, 46, 58-59, 73 and 75-77 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10, 24 of U.S. No. 11397029. Although the conflicting claims are not identical, they are not patentably distinct from each other because the invention of the prior art is an anticancer composition comprising: (i) a calcium phosphate comprising an amorphous calcium phosphate (ACP) or a poorly crystalline apatitic (PCA) calcium (-b-) (ii) an anticancer agent; and (iii) a physiologically acceptable fluid, wherein said composition is formulated as a formable or injectable paste that hardens in an endothermic reaction whereas the claims herein are a delivery composition comprising: a) calcium phosphate comprising an amorphous calcium phosphate (ACP) or a poorly crystalline apatitic (PCA) calcium

phosphate; and b) an antigen or vaccine wherein said calcium phosphate comprises greater than or equal to 40 wt% of said composition, and wherein said composition is formulated as an injectable paste that hardens in an endothermic reaction.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the paste comprising calcium phosphate material. The motivation comes from the teaching that the calcium phosphate material is a paste used in injectable or formable form. Hence a skilled artisan would have reasonable expectation of success in creating such a composition.

Claims 45, 46, 58-59, 73 and 75-77 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 6 of U.S. Patent No. US 6972130. Although the conflicting claims are not identical, they are not patentably distinct from each other because the invention of the prior art is a bioresorbable implant composition comprising: a calcium phosphate; a first agent that directly or indirectly stimulates osteoclast activity, wherein said first agent modulates the resorption of the calcium phosphate at an implant site; and a second agent that is biologically active, wherein said first and second agents are different whereas the claims herein are a delivery composition comprising: a) calcium phosphate comprising an amorphous calcium phosphate (ACP) or a poorly crystalline apatitic (PCA) calcium phosphate; and b) an antigen or vaccine wherein said calcium phosphate comprises greater than or equal to 40 wt% of said composition, and wherein said composition is formulated as an injectable paste that hardens in an endothermic reaction.

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate a vaccine or antigen into the composition. The motivation comes from the teaching that a biologically active agent is delivered using the ACP vehicle. Hence a skilled artisan would have reasonable expectation of success to incorporate the biologically active agents, vaccine or antigens.

Claims 45, 46, 58-59, 73 and 75-77 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. US 5650176. Although the conflicting claims are not identical, they are not patentably distinct from each other because the invention of the prior art is a method of preparing a poorly crystalline hydroxyapatite, comprising: providing a carbonated amorphous calcium phosphate material; removing at least a portion of the carbonate component from the carbonated amorphous calcium phosphate by thermal decomposition to form a decarbonated amorphous calcium phosphate; combining the decarbonated amorphous calcium phosphate and a second calcium phosphate in an aqueous medium without exothermic behavior, the second calcium phosphate and amorphous calcium phosphate present in a proportion to provide a Ca/P ratio characteristic of an apatitic calcium phosphate, whereby a hardened poorly crystalline hydroxyapatite is formed whereas the claims herein are a delivery composition comprising: a) calcium phosphate comprising an amorphous calcium phosphate (ACP) or a poorly crystalline apatitic (PCA) calcium phosphate; and b) an antigen or vaccine wherein said calcium phosphate comprises greater than or equal to 40 wt% of said

composition, and wherein said composition is formulated as an injectable paste that hardens in an endothermic reaction.

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate a vaccine or antigen into the composition. The motivation comes from the teaching that a biologically active agent (is useful -- see specification) is delivered with the ACP. Hence a skilled artisan would have reasonable expectation of success to incorporate the biologically active agents, vaccine or antigens.

Claims 45, 46, 58-59, 73 and 75-77 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. US 5683461. Although the conflicting claims are not identical, they are not patentably distinct from each other because the invention of the prior art is an injectable paste comprising: a decarbonated amorphous calcium phosphate prepared by removing by thermal decomposition at least a portion of a carbonate component from a carbonated amorphous calcium phosphate; a second calcium phosphate, the second calcium phosphate and amorphous calcium phosphate present in a proportion to provide a Ca/P ratio characteristic of an apatitic calcium phosphate; and an amount of aqueous medium sufficient to provide a paste of a desired consistency, characterized in that when in a moist tissue environment and upon reaching body temperature (37.degree. C.), the paste hardens into a poorly crystalline hydroxyapatite without exothermic behavior whereas the claims herein are a delivery composition comprising: a) calcium phosphate comprising an amorphous calcium phosphate (ACP) or a poorly crystalline apatitic (PCA) calcium phosphate; and b) an antigen or vaccine wherein said

calcium phosphate comprises greater than or equal to 40 wt% of said composition, and wherein said composition is formulated as an injectable paste that hardens in an endothermic reaction.

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate a vaccine or antigen into the composition. The motivation comes from the teaching that a biologically active agent is delivered using the ACP vehicle. Hence a skilled artisan would have reasonable expectation of success to incorporate the biologically active agents, vaccine or antigens.

Claims 45, 46, 58-59, 73 and 75-77 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-32 of U.S. Patent No. US 6027742. Although the conflicting claims are not identical, they are not patentably distinct from each other because the invention of the prior art is a composite material, comprising: (a) a strongly resorbable, poorly crystalline apatitic (PCA) calcium phosphate cement having an x-ray diffraction pattern similar to naturally occurring bone made by the process comprising: providing a paste comprised of amorphous calcium phosphate and water, whereby the paste hardens and converts to the poorly crystalline apatitic calcium phosphate, the poorly crystalline apatitic calcium phosphate characterized in that, at least about 80% is resorbed within one year when 1 g of the PCA calcium phosphate is placed in a rat intramuscular site; and (b) a biocompatible supplemental material, said material in intimate contact with the poorly crystalline material and present in an amount effective to impart a selected characteristic to the composite whereas the claims herein are a delivery composition comprising: a) calcium

phosphate comprising an amorphous calcium phosphate (ACP) or a poorly crystalline apatitic (PCA) calcium phosphate; and b) an antigen or vaccine wherein said calcium phosphate comprises greater than or equal to 40 wt% of said composition, and wherein said composition is formulated as an injectable paste that hardens in an endothermic reaction.

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate a vaccine or antigen into the composition. The motivation comes from the teaching that a biologically active agent is delivered using the ACP vehicle. Hence a skilled artisan would have reasonable expectation of success to incorporate the biologically active agents, vaccine or antigens.

Claims 45, 46, 58-59, 73 and 75-77 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. US 6117456. Although the conflicting claims are not identical, they are not patentably distinct from each other because the invention of the prior art is a reactive amorphous calcium phosphate material having at least 90% percent amorphous character and characterized in that, when prepared 1:1 as a mixture with dicalcium diphosphate in water, the mixture remains injectable and formable for a time greater than about 60 minutes at about 25.degree. C. and hardens at about 37.degree. C. within about 10 to about 60 minutes whereas the claims herein are a delivery composition comprising: a) calcium phosphate comprising an amorphous calcium phosphate (ACP) or a poorly crystalline apatitic (PCA) calcium phosphate; and b) an antigen or vaccine wherein said calcium phosphate comprises greater than or equal to

40 wt% of said composition, and wherein said composition is formulated as an injectable paste that hardens in an endothermic reaction.

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate a vaccine or antigen into the composition. The motivation comes from the teaching that a biologically active agent is delivered using the ACP vehicle. Hence a skilled artisan would have reasonable expectation of success to incorporate the biologically active agents, vaccine or antigens.

Claims 45, 46, 58-59, 73 and 75-77 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-30 of U.S. Patent No. US 6139578. Although the conflicting claims are not identical, they are not patentably distinct from each other because the invention of the prior art is a method for preparing a therapeutic, structural or cosmetic implant, comprising: a. providing a composition in hydrated precursor form, wherein the hydrated precursor is capable of conversion into a hardened poorly crystalline apatitic (PCA) calcium phosphate; b. promoting conversion of the hydrated precursor so that the composition becomes hardened PCA calcium phosphate; and c. introducing at least one cell into the composition prior to hardening of the hydrated precursor whereas the claims herein are a delivery composition comprising: a) calcium phosphate comprising an amorphous calcium phosphate (ACP) or a poorly crystalline apatitic (PCA) calcium phosphate; and b) an antigen or vaccine wherein said calcium phosphate comprises greater than or equal to 40 wt% of said composition, and wherein said composition is formulated as an injectable paste that hardens in an endothermic reaction.

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate a vaccine or antigen into the composition. The motivation comes from the teaching that a biologically active agent is delivered using the ACP vehicle. Hence a skilled artisan would have reasonable expectation of success to incorporate the biologically active agents, vaccine or antigens.

Claims 45, 46, 58-59, 73 and 75-77 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. US 6331312. Although the conflicting claims are not identical, they are not patentably distinct from each other because the invention of the prior art is a method of preparing a calcium deficient apatitic calcium phosphate composite material, comprising: mixing in any order, (a) a calcium source consisting essentially of an amorphous calcium phosphate (ACP), (b) a passive promoter, and (c) a supplementary material selected to alter tensile strength and hardness, alter fracture toughness alter elasticity, alter resorption characteristics, provide imaging capacity, or alter flow properties and setting times of the composite, the supplementary material present in an amount effective to impart the selected characteristic to the composite; and initiating conversion of the amorphous calcium phosphate into a calcium deficient apatitic calcium phosphate whereas the claims herein are a delivery composition comprising: a) calcium phosphate comprising an amorphous calcium phosphate (ACP) or a poorly crystalline apatitic (PCA) calcium phosphate; and b) an antigen or vaccine wherein said calcium phosphate comprises greater than or equal to 40 wt% of said composition, and

wherein said composition is formulated as an injectable paste that hardens in an endothermic reaction.

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate a vaccine or antigen into the composition. The motivation comes from the teaching that a biologically active agent is delivered using the ACP vehicle. Hence a skilled artisan would have reasonable expectation of success to incorporate the biologically active agents, vaccine or antigens.

Claims 45, 46, 58-59, 73 and 75-77 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 of U.S. Patent No. US 6132463. Although the conflicting claims are not identical, they are not patentably distinct from each other because the invention of the prior art is a method of growing bone in vivo comprising: a. providing a hydrated precursor comprising: i. at least one amorphous calcium phosphate (ACP); ii. at least one bone-forming cell; and iii. a sufficient amount of aqueous solution so that the hydrated precursor has a consistency selected from the group consisting of a paste consistency and a putty consistency which consistency is maintained at ambient temperature for a period of time at least 60 minutes long, the aqueous solution being compatible with the at least one bone-forming cell; b. introducing the hydrated precursor into a bony site; and c. allowing the hydrated precursor to harden. 2. A method of growing bone in vivo comprising: a. providing a hydrated precursor comprising: i. at least one amorphous calcium phosphate (ACP); and ii. a sufficient amount of aqueous solution so that the hydrated precursor has a consistency, which consistency is maintained at ambient temperature

for a period of time at least 60 minutes long, selected from the group consisting of a paste consistency and a putty consistency; b. introducing the hydrated precursor into a bony site; c. promoting conversion of the ACP into a PCA calcium phosphate before or after the step of introducing; and d. allowing bone-forming cells to enter the implanted material whereas the claims herein are a delivery composition comprising: a) calcium phosphate comprising an amorphous calcium phosphate (ACP) or a poorly crystalline apatitic (PCA) calcium phosphate; and b) an antigen or vaccine wherein said calcium phosphate comprises greater than or equal to 40 wt% of said composition, and wherein said composition is formulated as an injectable paste that hardens in an endothermic reaction.

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate a vaccine or antigen into the composition. The motivation comes from the teaching that a biologically active agent is delivered using the ACP vehicle. Hence a skilled artisan would have reasonable expectation of success to incorporate the biologically active agents, vaccine or antigens.

Claims 45, 46, 58-59, 73 and 75-77 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-27 of U.S. Patent No. US 6277151. Although the conflicting claims are not identical, they are not patentably distinct from each other because the invention of the prior art is a method of growing cartilage in vivo comprising: a. providing a hydrated precursor comprising: i. at least one amorphous calcium phosphate (ACP); ii. at least one cartilage-forming cell or precursor thereof; and iii. a sufficient amount of aqueous solution so that the hydrated

precursor has a consistency selected from the group consisting of a paste consistency and a putty consistency, the aqueous solution being compatible with the at least one cartilage-forming cell or precursor thereof; b. introducing the hydrated precursor into a site in vivo; and c. after step a, allowing the hydrated precursor to harden whereas the claims herein are a delivery composition comprising: a) calcium phosphate comprising an amorphous calcium phosphate (ACP) or a poorly crystalline apatitic (PCA) calcium phosphate; and b) an antigen or vaccine wherein said calcium phosphate comprises greater than or equal to 40 wt% of said composition, and wherein said composition is formulated as an injectable paste that hardens in an endothermic reaction.

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate a vaccine or antigen into the composition. The motivation comes from the teaching that a biologically active agent is delivered using the ACP vehicle. Hence a skilled artisan would have reasonable expectation of success to incorporate the biologically active agents, vaccine or antigens.

Claims 45, 46, 58-59, 73 and 75-77 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-32 of U.S. Patent No. US 6544290. Although the conflicting claims are not identical, they are not patentably distinct from each other because the invention of the prior art is cell-scaffold composition prepared in vitro for use as a biocompatible implant, comprising: i) a three-dimensional scaffold comprising a hydrated precursor that comprises amorphous calcium phosphate that is capable of being converted into a synthetic poorly crystalline apatitic calcium phosphate; and ii) at least one cell attached in vitro to the surface of the

scaffold whereas the claims herein are a delivery composition comprising: a) calcium phosphate comprising an amorphous calcium phosphate (ACP) or a poorly crystalline apatitic (PCA) calcium phosphate; and b) an antigen or vaccine wherein said calcium phosphate comprises greater than or equal to 40 wt% of said composition, and wherein said composition is formulated as an injectable paste that hardens in an endothermic reaction.

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate a vaccine or antigen into the composition. The motivation comes from the teaching that a biologically active agent (is useful -- see specification) is delivered with the ACP. Hence a skilled artisan would have reasonable expectation of success to incorporate the biologically active agents, vaccine or antigens.

Claims 45, 46, 58-59, 73 and 75-77 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. US 7150879. Although the conflicting claims are not identical, they are not patentably distinct from each other because the invention of the prior art is a formable paste, suitable for use as a bone substitution material, comprising a mixture of: (a) a powder component, comprising: (i) an amorphous calcium phosphate having a Ca/P molar ratio between 1.1 and 1.55, wherein said amorphous calcium phosphate is present in an amount greater than 20 wt % of said powder component, and (ii) a second, crystalline calcium phosphate; and (b) a physiologically acceptable fluid in an amount to provide a paste having a formable or injectable consistency, wherein the amorphous calcium phosphate and the second calcium phosphate, in combination,

have a stoichiometry that permits formation of a calcium-deficient, poorly crystalline apatitic (PCA) calcium phosphatewhereas the claims herein are a delivery composition comprising: a) calcium phosphate comprising an amorphous calcium phosphate (ACP) or a poorly crystalline apatitic (PCA) calcium phosphate; and b) an antigen or vaccine wherein said calcium phosphate comprises greater than or equal to 40 wt% of said composition, and wherein said composition is formulated as an injectable paste that hardens in an endothermic reaction.

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate a vaccine or antigen into the composition. The motivation comes from the teaching that a biologically active agent is delivered using the ACP vehicle. Hence a skilled artisan would have reasonable expectation of success to incorporate the biologically active agents, vaccine or antigens.

Claims 45, 46, 58-59, 73 and 75-77 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. US 6953594. Although the conflicting claims are not identical, they are not patentably distinct from each other because the invention of the prior art is a self-hardening calcium phosphate composite, comprising: an amorphous calcium phosphate; a second calcium phosphate having a calcium to phosphorous atomic ratio (Ca:P) of less than or equal to 1.67, wherein the amorphous calcium phosphate and the second calcium phosphate in combination have a calcium to phosphorous atomic ratio in the range of 1.1 to 1.9; a supplemental material, said supplemental material comprising demineralized bone matrix; and a carrier fluid in an amount sufficient to form

a paste or putty whereas the claims herein are a delivery composition comprising: a) calcium phosphate comprising an amorphous calcium phosphate (ACP) or a poorly crystalline apatitic (PCA) calcium phosphate; and b) an antigen or vaccine wherein said calcium phosphate comprises greater than or equal to 40 wt% of said composition, and wherein said composition is formulated as an injectable paste that hardens in an endothermic reaction.

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate a vaccine or antigen into the composition. The motivation comes from the teaching that a biologically active agent is delivered using the ACP vehicle. Hence a skilled artisan would have reasonable expectation of success to incorporate the biologically active agents, vaccine or antigens.

Claims 45, 46, 58-59, 73 and 75-77 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-36 of U.S. Patent No. US 7517539. Although the conflicting claims are not identical, they are not patentably distinct from each other because the invention of the prior art is a method of preparing a bioceramic composition, comprising the following steps: a) dry mixing powders of a calcium phosphate and a promoter; b) prior to hydration of said dry powders prepared in step (a), pressing said dry powders to form a compressed object of a predetermined shape; and c) hydrating said compressed object of step (b) to form a reaction product, said reaction product comprising a poorly crystalline apatitic calcium phosphate whereas the claims herein are a delivery composition comprising: a) calcium

phosphate comprising an amorphous calcium phosphate (ACP) or a poorly crystalline apatitic (PCA) calcium phosphate; and b) an antigen or vaccine wherein said calcium phosphate comprises greater than or equal to 40 wt% of said composition, and wherein said composition is formulated as an injectable paste that hardens in an endothermic reaction.

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate a vaccine or antigen into the composition. The motivation comes from the teaching that a biologically active agent (is useful -- see specification) is delivered with the ACP. Hence a skilled artisan would have reasonable expectation of success to incorporate the biologically active agents, vaccine or antigens.

Claims 45, 46, 58-59, 73 and 75-77 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-40 of U.S. Patent No. US 6840961. Although the conflicting claims are not identical, they are not patentably distinct from each other because the invention of the prior art is a bone implant comprising an unhydrated calcium phosphate precursor capable of forming poorly-crystalline hydroxyapatite in vivo upon hydration at the implantation site, wherein the precursor has a calcium to phosphorous atomic ratio between about 1.2 and about 1.68, and wherein the implant has a compressive strength of at least about 60 MPa whereas the claims herein are a delivery composition comprising: a) calcium phosphate comprising an amorphous calcium phosphate (ACP) or a poorly crystalline apatitic (PCA) calcium phosphate; and b) an antigen or vaccine wherein said calcium phosphate comprises greater than or equal to 40 wt% of said composition, and wherein

said composition is formulated as an injectable paste that hardens in an endothermic reaction.

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate a vaccine or antigen into the composition. The motivation comes from the teaching that a biologically active agent (is useful -- see specification) is delivered with the ACP. Hence a skilled artisan would have reasonable expectation of success to incorporate the biologically active agents, vaccine or antigens.

Claims 45, 46, 58-59, 73 and 75-77 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-27 of U.S. Patent No. US 6287341. Although the conflicting claims are not identical, they are not patentably distinct from each other because the invention of the prior art is a method of preparing a ceramic implant, comprising: mixing in any order, (a) a reactive amorphous calcium phosphate (b) a second calcium phosphate wherein the second calcium phosphate has a calcium to phosphate ratio of less than or equal to 1.67, and (c) a physiological liquid, said liquid in the amount to provide a paste or putty; and introducing the paste or putty into an implant site whereas the claims herein are a delivery composition comprising: a) calcium phosphate comprising an amorphous calcium phosphate (ACP) or a poorly crystalline apatitic (PCA) calcium phosphate; and b) an antigen or vaccine wherein said calcium phosphate comprises greater than or equal to 40 wt% of said composition, and wherein said composition is formulated as an injectable paste that hardens in an endothermic reaction.

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate a vaccine or antigen into the composition. The motivation comes from the teaching that a biologically active agent is delivered using the ACP vehicle. Hence a skilled artisan would have reasonable expectation of success to incorporate the biologically active agents, vaccine or antigens.

Claims 45, 46, 58-59, 73 and 75-77 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-41 of U.S. Patent No. US 5783217. Although the conflicting claims are not identical, they are not patentably distinct from each other because the invention of the prior art is a method of preparing a low crystallinity calcium phosphate apatite, comprising: precipitating a low crystallinity calcium phosphate from an aqueous solution comprising calcium and phosphate ions; collecting the low crystallinity calcium phosphate from the solution; and dehydrating the low crystallinity calcium phosphate in a relative humidity of less than 100% and at a temperature to obtain a low crystallinity calcium phosphate apatite block solid whereas the claims herein are a delivery composition comprising: a) calcium phosphate comprising an amorphous calcium phosphate (ACP) or a poorly crystalline apatitic (PCA) calcium phosphate; and b) an antigen or vaccine wherein said calcium phosphate comprises greater than or equal to 40 wt% of said composition, and wherein said composition is formulated as an injectable paste that hardens in an endothermic reaction.

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate a vaccine or antigen into the composition. The motivation

comes from the teaching that a biologically active agent (is useful -- see specification) is delivered with the ACP. Hence a skilled artisan would have reasonable expectation of success to incorporate the biologically active agents, vaccine or antigens.

Claims 45, 46, 58-59, 73 and 75-77 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. US 5258044. Although the conflicting claims are not identical, they are not patentably distinct from each other because the invention of the prior art is method for preparing a coated implant, said method comprising the steps of: (a) providing a gel of amorphous calcium phosphate having a molar ratio of calcium to phosphorous of 0.5 to 1.6; (b) dispersing said gel of amorphous calcium phosphate in an aqueous liquid to form a colloidal mixture of said amorphous calcium phosphate and said aqueous liquid which comprises between 60% and 99% by weight water; (c) immersing an implant to be coated in said colloidal mixture; and (d) with said implant used as an anode, electrodepositing said amorphous calcium phosphate on said implant to form a substantially uniform coating whereas the claims herein are a delivery composition comprising: a) calcium phosphate comprising an amorphous calcium phosphate (ACP) or a poorly crystalline apatitic (PCA) calcium phosphate; and b) an antigen or vaccine wherein said calcium phosphate comprises greater than or equal to 40 wt% of said composition, and wherein said composition is formulated as an injectable paste that hardens in an endothermic reaction.

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate a vaccine or antigen into the composition. The motivation

comes from the teaching that a biologically active agent (is useful -- see specification) is delivered with the ACP. Hence a skilled artisan would have reasonable expectation of success to incorporate the biologically active agents, vaccine or antigens.

Response to Arguments

Applicant's arguments filed June 17, 2011 have been fully considered.

With respect to Applicant's argument that the paste does not harden in an endothermic reaction; the Examiner states that such hardening will occur because the prior art teaches the same composition as claimed. Further, the general teaching of a calcium phosphate reads on the ACP or PCA calcium phosphate.

Applicant argues that Gerhart describes bone cement that is cured in an exothermic reaction as opposed to the present claims which harden in an endothermic reaction. Applicants provide a Declaration to explain the difference between Gerhart and the present invention. Applicants and the Tofighi Declaration focus on the Gerhart composition which cures in a mildly exothermic reaction. Applicants argue that the endothermic reaction of the present invention was an unexpected property of the calcium phosphate.

The arguments by Applicant, the Tofighi Declaration, and Strunk Declaration are herein acknowledged. However, it should be noted that Antonucci and Gerhart were not the primary references. Gerhart was not used for the teaching of the paste hardening in an endothermic reaction. Further, the claims are drawn to a composition and the process of the paste hardening in an endothermic reaction is a property of the

composition. Gerhart was used for the teaching of delivering a pharmaceutical agent in a calcium phosphate composition. Therefore, the rejections are deemed proper.

The arguments are not persuasive.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Soroush whose telephone number is (571)272-5008. The examiner can normally be reached on Monday through Friday from 8:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627